TO STUDY AND EVALUATE DIASTOLIC DYSFUNCTION IN PATIENTS OF ALCOHOLIC AND NON-ALCOHOLIC CIRRHOSIS

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ABSTRACT

BACKGROUND

Cardiovascular dysfunction is the major component of morbidity in patients of liver cirrhosis and a cardinal prognostic indicator in patients undergoing liver transplantation. The constellation of hyperdynamic circulation, peripheral vasodilation and volume overload alters the systolic and diastolic dysfunction leading to cirrhotic cardiomyopathy (CCM). In this study, we evaluated and compared the diastolic dysfunction among alcoholic and non-alcoholic cirrhotic patients.

AIMS

1) To Study the Prevalence of Diastolic Dysfunction in Alcoholic & Non-Alcoholic Cirrhotics and Controls. 2) To Compare the Diastolic functional status between alcoholic and non-alcoholic cirrhosis patients.

MATERIALS AND METHODS

A cross-sectional case control study was conducted in 100 male cirrhotic patients consisting of alcoholic and non-alcoholic cirrhotic subjects with age matched 50 controls in Pt. JNM Medical College & Dr. BRAM Hospital, Raipur. Left ventricular diastolic dysfunction was assessed using echocardiographic parameters.

STATISTICAL ANALYSIS

The range, median, standard deviation and statistical significance were calculated. Most of the data is analysed by Student T-test, Mann Whitney U test, while the data with frequency distribution is analysed by Fisher's exact. With p value < 0.05, the correlation was significant.

RESULTS

Among all cirrhotics, 49% had diastolic dysfunction (DD) in comparison to 22% controls which was statistically significant ($p<0.05$). 50% of the alcohol cirrhotic had DD compared with 25% of controls which was significant ($p<0.05$) & 46% non-alcoholic cirrhosis patients had DD compared with 26% in the control group which was statistically significant ($p<0.05$). 50% of alcoholic cirrhotics had DD compared with 29 (46%) non-alcoholic cirrhotic patients which was not statistically significant ($p>1$).

CONCLUSION

Our study showed that patients with alcoholic and non-alcoholic cirrhosis have higher occurrence of DD (49% and 46% respectively) than controls owing to alterations in the myocardial contractile and relaxation function. It also shows that although DD is a frequent event in cirrhosis, it is usually of mild degree and does not correlate with severity of liver dysfunction. There were no significant differences in diastolic parameters between alcoholic and non-alcoholic cirrhosis concluding that alcohol likely plays a non-significant role in cardiovascular dysfunction in cirrhotics.

KEYWORDS

Diastolic Dysfunction (LVDD), Cirrhotic Cardiomyopathy (CCM).

HOW TO CITE THIS ARTICLE: Padia GS, Lakra D, Khare RL. To study and evaluate diastolic dysfunction in patients of alcoholic and non-alcoholic cirrhosis. J. Evid. Based Med. Healthc. 2016; 3(35), 1683-1686. DOI: 10.18410/jebmh/2016/377

INTRODUCTION: Cirrhosis is defined pathologically as a diffuse process with fibrosis and nodule formation.[1] It represents the late stage of progressive hepatic fibrosis characterised by distortion of the hepatic architecture and the formation of regenerative nodules. Common causes of cirrhosis include:[2] Chronic viral hepatitis (hepatitis B, C), Alcoholic liver disease, Non-alcoholic fatty liver disease, Hemochromatosis. According to the Global Burden of Disease 2010 study, liver cirrhosis caused 31 million Disability Adjusted Life Years (DALYs), or 1.2% of global DALYs, in 2010, and one million deaths, or 2% of all deaths worldwide in that year.[3] According to the latest WHO data published in May 2014 Liver Disease Deaths in India reached

Financial or Other, Competing Interest: None.
Submission 29-03-2016, Peer Review 16-04-2016,
Acceptance 22-04-2016, Published 30-04-2016.
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DOI: 10.18410/jebmh/2016/377

216,865 or 2.44% of total deaths. The age adjusted death rate is 21.96 per 100,000 of population ranks India #61 in the world.

Cardiovascular alterations are frequently observed in the late stages of cirrhosis. The patient with hepatocellular dysfunction in cirrhosis shows marked vasodilatation accompanied by hyper dynamic circulation and opening of arteriovenous shunts, it has been established that the cardiac response to physiologic and pharmacologic stresses may be impaired in many different types of cirrhosis. This finding has resulted in the recognition that a unique form of high output cardiac dysfunction occurs in liver disease. Clinically, cardiac dysfunction is often mild or latent in cirrhosis, a finding some have attributed to the after load reducing effects of systemic vasodilatation that decrease cardiac work.[4] However, in the setting of increased cardiac stress such as liver transplantation[5] and TIPS overt cardiac dysfunction may occur. Perioperative cardiac dysfunction has been observed in up to 50 percent of patients after transplantation,[5] with overt heart failure occurring in 1 percent to 2 percent of patients. However, cardiac failure is a cause of mortality in up to 7 percent to 20 percent of transplants recipients. It is now clear that patients with end-stage liver disease are at increased risk of acute coronary occlusion, myocardial failure, arrhythmia and complete cardiovascular collapse following transplantation compared to other major surgical procedures.

However, there is no consensus on how to efficiently detect cardiovascular disease in asymptomatic patients prior to transplantation or to determine what risk a transplant candidate with heart disease has of suffering from a serious perioperative adverse event. Without this information, it is difficult to determine what type or severity of heart disease should exclude a patient from transplantation. Routine screening of transplant candidates with echocardiography is an effective way to identify comorbid cardiac disease. Hence it is relevant to perform a detailed study of cardiovascular system in cirrhosis patients.

MATERIALS AND METHODS: This was a Case Control Analytical study carried out at Pt. JNM Medical College & DR. BRAM Hospital, Raipur [C.G] in the Department of Medicine during June 2014 to Oct. 2015. Ethical clearance was obtained and the study was initiated. Informed consent was obtained before taking up the case for study.

1) **Inclusion Criteria**: All newly diagnosed cases of cirrhosis of liver based on physical examination, biochemical parameters, ultra-sonogram of abdomen.

2) **Exclusion Criteria:** Female patients and patients below 20 years and above 60 years were excluded; likewise, patients with major cardiovascular, haematological, infective, metabolic complications were excluded from the study.

3) **Doppler Echocardiography**: In Doppler study, following values was evaluated. 1. E-peak velocity 2. A-peak velocity 3. E/A ratio. 4. LVDd, LVDs, LVPWd, LVPWs, IVSd, IVRT, DT.

STATISTICAL ANALYSIS: The range, median, standard deviation and statistical significance were calculated. Most of the data is analysed by Student T-test, Mann Whitney U test, while the data with frequency distribution is analysed by Fisher's exact. Wherever p value was found to be less than 0.05, it was considered significant.

OBSERVATIONS:

Pattern of diastolic dysfunction	Alcoholic cirrhosis patients (n=38)	Non-alcoholic cirrhosis pts.(n=62)	Controls (n=40)
Impaired relaxation pattern	13(34%)	15(24%)	6(15%)
Pseudo-normal pattern	4(11%)	7(11%)	2(5%)
Restrictive pattern	2(5%)	7(11%)	2(5%)
Total	**19(50%)**	**29(46%)**	**10(25%)**

Table 1: Left Ventricular Diastolic Dysfunction Patterns in Cirrhosis Patients

Parameter	Cases	Mean	SD	P value
DT	Alc-cirrhotics	145.947	37.557	<0.001
	Controls	203.525	4.0128	
IVRT	Alc-cirrhotics	98.683	26.603	<0.001
	Controls	79.6	14.486	
E/A	Alc-cirrhotics	1.2485	0.3774	0.067
	Controls	1.128	0.1534	

Table 2: Comparison of Diastolic Dysfunction Between Alcoholic and Controls

Parameter	Cases	Mean	SD	P value
DT	Non-alc. Cirrhotics	145.94	44.33	<0.001
	Controls	203.53	4.03	
IVRT	Non-alc. Cirrhotics	100.58	27.23	<0.001
	Controls	79.6	14.49	
E/A	Non-alc. Cirrhotics	1.49	0.52	<0.001
	Controls	1.128	0.16	

Table 3: Comparison of Diastolic Dysfunction Between Non-alcoholic and Controls

Parameter	Cases	Mean	SD	p value
DT	Alc. Cirrhotics	145.947	37.56	0.816
	Non-alc. Cirrhotics	145.934	44.35	
IVRT	Alc. Cirrhotics	98.685	26.61	0.735
	Non-alc. Cirrhotics	100.573	27.23	
E/A	Alc. Cirrhotics	1.2485	0.38	0.011
	Non-alc. Cirrhotics	1.482	0.52	

Table 4: Comparison of Diastolic Dysfunction Between Alcoholic and Non-alcoholic Cirrhotics

RESULTS: Majority of patients in both groups with diastolic dysfunction showed LV relaxation abnormally pattern (>50%) (Stage 1 diastolic dysfunction).

1. 48 cirrhotic patients (48%) had diastolic dysfunction (DD) compared to 10 persons (25%) in the control group which was statistically significant ($p<0.05$) [The Standard Error of Difference (SED) was 8.47 while the Observed Difference (OD) was 23].
2. 19 patients (50%) of the alcohol cirrhotic had DD compared with 10 (25%) individuals of controls which was significant ($p<0.05$) [SED was 8.11 while the OD was 25].
3. 29 (46%) non-alcoholic cirrhosis patients had DD compared with 10 (25%) individuals in the control group which was statistically significant ($p<0.05$) [SED was 9.32 while the OD was 21].
4. 19 patients (50%) of alcoholic cirrhotics had DD compared with 29 (46%) non-alcoholic cirrhotic patients which was not significant ($p>1$) [SED was 10.28 while OD was only 4].
5. Diastolic dysfunction was dictated by reduction of deceleration time, impaired isovolumic relaxation time and increased E/A ratio. In comparison between alc. cirrhotics and controls, DT and IVRT was impaired than in controls which a significant co-relation ($p< 0.001$). Among alc. cirrhotics and controls, there was no statistical difference in E/A ($p< 0.67$).
6. In comparison to alc. cirrhotics, non alc. cirrhotics showed impairment in all the three parameters of diastolic dysfunction and this was statistically significant ($p< 0.001$) when compared to controls.
7. There was no statistically significant difference between diastolic dysfunction of alc. and non-alc. cirrhotics in all the parameters of diastolic dysfunction. ($p>0.05$)

DISCUSSION: Cirrhosis of liver involves most organs and systems; hence it may be considered as a systemic disease.[6] Knowledge of cardiovascular system involvement in a cirrhotic patient is important in planning treatment and assessing the prognosis.

Analysis of age and gender wise distribution of cases: In this study, out of total 140 patients, 40 patients were taken as controls, 100 were cases of which 38(38%) were alcoholic cirrhotics and 62% were non-alcoholic cirrhotics. Patients between 20-40 yrs. age were 3(8%) were alcoholic cirrhotics, 38(56%) were non-alcoholic cirrhotics and 16(40%) were controls. Between 41-60 yrs. there were 35(92%) alcoholic cirrhotics, 24(44%) were non-alcoholic cirrhotics and 24(60%) were controls. Both young and old patients with alcoholic and non-alcoholic cirrhosis were involved in the study. The mean age in this study was 45 yrs.

Analysis of Left ventricular diastolic function: In a normal heart, during diastole, an initial active phase of relaxation and a later passive phase of filling are present. In the relaxation phase; a series of energy consuming steps occur which are mediated by hydrolysis of ATP. In the latter filling phase, several complex interactions occur like diastolic suction, passive filling, pericardial restraint, ventricular interaction.[6] And visco-elastic forces of the myocardium which determines the 'effective operating left ventricular chamber compliance. In the present study, left ventricular (LV) diastolic function was studied in depth using parameters like isovolumic relaxation time, mitral inflow velocity pattern and mitral E deceleration time. Cirrhosis patients showed an increased occurrence of diastolic dysfunction compared to controls. This finding was seen in alcoholic and non-alcoholic patients. Majority of patients showed an impaired LV relaxation pattern indicating that the initial energy consuming step is being affected in cirrhosis.

Similar observation was documented earlier by Alexander et al.[7] A few patients showed advanced diastolic dysfunction in the form of restrictive pattern. This usually occurs when the passive stiffness of heart is affected by diffuse fibrosis or when the myocytes are hypertrophied. So heart may also be influenced by growth factors which mediate fibrosis in liver. However, there was no significant difference between the occurrence and pattern of diastolic dysfunction among alcoholic and non–alcoholic cirrhosis patients.

In study by Piyush O. Somani, Qais contractor,[8] Diastolic dysfunction was unrelated to age; sex and aetiology of cirrhosis. There was no significant difference between the diastolic parameters among alcoholic and non-alcoholic cirrhotics. There was evidence of diastolic dysfunction in both the groups of cirrhotic patients, as indicated by statistically significant prolongation of deceleration time compared to the controls. The E/A ratio, the other parameter of diastolic dysfunction, did not show a statistically significant difference in our study.

CONCLUSION: Patients with alcoholic and non-alcoholic cirrhosis have higher occurrence of diastolic dysfunction (50% and 46% respectively) than controls which was statistically significant. This observation runs in parallel to other published data.

Variable observations noted in the present study may likely be related to the rigid criteria adopted in case selection and possibly due to genetic or ethnic difference as well as their susceptibility.

Present study demonstrated that Indian patients with cirrhosis do have diastolic dysfunction. In the absence of other risk factors for cardiac disease, this dysfunction could be attributed only to cirrhotic cardiomyopathy. It also shows that although diastolic dysfunction is a frequent event in cirrhosis, it is usually of mild degree and does not correlate with severity of liver dysfunction. There were no significant differences in echocardiographic parameters between alcoholic and non-alcoholic cirrhosis.

In view of the above conclusions, it is suggested to take up a prospective study with long term follow-up with and without modern cardioprotective agents in order to find out the effective interventions which minimise the progression of cirrhosis and subsequent cardiac dysfunction.

REFERENCES:

1. Ian D Penman. Davidson's Principles and practice of medicine. Cirrhosis and chronic liver failure: Churchill Living stone Chapter 842, 2002;19th edn:848-852.
2. Heidelbaugh JJ, Bruderly M. Cirrhosis and chronic liver failure: part 1. Diagnosis and evaluation. Am Fam Physician 2006;74(5):756-762.
3. Murray CJ, Vos T, Lozano R, et al Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380(9859):2197-2223.
4. Ma Z, Lee S. Cirrhotic cardiomyopathy, getting to the heart of the matter. Hepatology 1996;24(2):451-459.
5. Danovan CL, Marcovitz PA, Punch JD, et al. Two dimensional and dobutamine stress echocardiography in the pre-operative assessment of patients with end-stage liver disease prior to orthotopic liver transplantation. Transplantation 1996;61(8):1180-1188.
6. Gatta A, Merkel C, Sacerdoti D, et al. Cardiac involvement in liver cirrhosis. Ann Ital Med int 1993;8(4):244-247.
7. Alexander J, Nutan Desai, Peeyush Mishra, et al. Cirrhotic cardiomyopathy in Indian subject. Journal of Gastroenterology and Hepatology 2007;22(3):395-399
8. Piyush O Somani, Qais contractor, Ajay S Chaurasia, et al. Diastolic dysfunction characterizes cirrhotic cardiomyopathy. Indian Heart Journal 2014;66(6):649-655.